# UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|---|---|---|---|---|
| 09/930,020 | 08/14/2001 | Kurt C. Gish | 018501-003100US | 2304 |

27194 7590 11/15/2004

HOWREY SIMON ARNOLD & WHITE, LLP
C/O M.P. DROSOS, DIRECTOR OF IP ADMINISTRATION
2941 FAIRVIEW PK
BOX 7
FALLS CHURCH, VA 22042

| EXAMINER | |
|---|---|
| RAWLINGS, STEPHEN L | |
| **ART UNIT** | **PAPER NUMBER** |
| 1642 | |

DATE MAILED: 11/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 09/930,020 | GISH ET AL. | |
| | Examiner | Art Unit | |
| | Stephen L. Rawlings, Ph.D. | 1642 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *17 August 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *32, 38-40, and 42-68* is/are pending in the application.

4a) Of the above claim(s) *60-68* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *32,38-40 and 42-59* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

**Application Papers**

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

## DETAILED ACTION

1. The amendment filed August 17, 2004 is acknowledged and has been entered. Claims 1-6, 8-31, 33-37, and 41 have been canceled. Claims 32, 38, and 44 have been amended. Claims 45-59 have been added.

2. Claims 32, 38-40, and 42-68 are pending in the application. Claims 60-68 have been withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected invention, there being no allowable generic or linking claim.

3. Claims 32, 38-40, and 42-59 are currently under prosecution.

4. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

5. The following Office action contains NEW GROUNDS of rejection necessitated by amendment.

### Grounds of Objection and Rejection Withdrawn

6. Unless specifically reiterated below, Applicant's amendment and/or arguments set forth in the amendment filed August 17, 2004 have obviated or rendered moot the grounds of objection and rejection set forth in the previous Office action mailed February 26, 2004.

### *Election/Restrictions*

7. Newly submitted claims 60-68 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons:

Claims 60-68 are drawn to a method for monitoring colorectal cancer in a human patient, whereas the elected invention is a method for diagnosing colorectal cancer. The inventions of claims 60-68 are patentably distinct from the elected invention

because these inventions have a different purpose. The inventions of claims 60-68 monitor the progression, or lack thereof, of colorectal cancer in a patient previously diagnosed with the disease and the elected invention is a method for diagnosing the incidence, onset, or presence of colorectal cancer in a patient. Therefore, although both inventions comprise the step of measuring the level of expression of a particular gene, the inventions of claims 60-68 comprise correlating this determined level of expression with the progression, or lack thereof, of an established colorectal cancer in a patient, whereas the elected invention comprises correlating the determined level of expression with the incidence, onset, or presence of the disease. Because these methods have different objectives and comprise establishment of different correlations, the inventions have acquired a separate status in the art. For all of the above reasons, the search required to examine the invention of claims 60-68 is not the same as, nor is it coextensive with the search that was performed to examine claims drawn to the elected invention. Accordingly, examination of claims 60-68 would require a new and different search to be performed. The need to perform an additional search would unduly burden the Examiner. Because the inventions of claims 60-68 are patentably distinct from the elected invention, and because both inventions could not be searched and examined without serious burden, the restriction to the elected invention is proper.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 60-68 have withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

***Grounds of Rejection Maintained***

***Claim Rejections - 35 USC § 101***

8. The rejection of claims 32, 38-40, and 42-59 under 35 U.S.C. § 101, because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reason set forth in section 12 of the previous Office action mailed February 26, 2004 is maintained.

At pages 19-21 of the amendment filed August 17, 2004, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Although Applicant has traversed this ground of rejection, it appears that Applicant has not rebutted the primary issue at hand, namely that the specification does not teach whether the gene encoding the CBF9 polypeptide of SEQ ID NO: 2 is over- or under-expressed in colorectal cancer cells, as compared to normal colorectal cancer cells. Applicant has argued that the disclosure implies the gene encoding the CBF9 polypeptide of SEQ ID NO: 2 is overexpressed in colorectal cancer, but, as noted in the previous Office action, while Table 1 lists the genes that Applicant found to be overexpressed in colorectal cancer cells, the gene encoding CBF9 (Unigene No. Hs.157601; GenBank™ Accession No. AC05383) does not appear to be included in this list. The specification does not explicitly teach whether the gene encoding CBF9 is overexpressed in colorectal cancer cells; consequently, given only the information provided in the instant disclosure of the claimed invention, the skilled artisan could not immediately use the claimed invention.

Furthermore, as also noted in the previous Office action, the instant application provides a description of a polynucleotide sequence, namely SEQ ID NO: 1, which appears to be the sequence of the "CBF9 gene". The table at page 109 appears to list the Genbank™ accession number of the sequence set forth therein; however, it is duly noted Genbank™ Accession No. AC005383 differs markedly from the sequence set

forth in Table 2. Genbank™ Accession No. AC005383 is the 1,217,714 residue polynucleotide sequence of a cloned fragment of human chromosome 10, whereas SEQ ID NO: 1 is only 3,375 nucleotides in length. Because Applicant has not addressed this issue in the response filed August 17, 2004, this apparent discrepancy remains unresolved.

***Claim Rejections - 35 USC § 112***

9. Claims 32, 38-40, and 42-59 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth in section 9 above, one skilled in the art clearly would not know how to use the claimed invention.

At page 22 of the amendment filed August 17, 2004, Applicant has stated that this ground of rejection is traversed for the reasons provided in traversing the rejection of the claims under 35 USC § 101 as lacking a specific and substantial asserted utility or a well established utility.

Applicant's arguments have been carefully considered but not found persuasive for the same reasons Applicant's traversal of the rejection of the claims under 35 USC § 101 has not been found persuasive; and those reasons are set forth above.

10. If the grounds of rejection of the claims under 35 USC §§ 101 and 112, first paragraph for the reasons set forth in sections 9 and 10, respectively, were to be obviated, claims 32, 38-40, 42, 43, 45-56 would still be rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for practicing the methods of claims 32, 38-40, 42, 43, 45-56, wherein said method comprises determining the expression of a nucleic acid molecule comprising SEQ ID NO: 1 or an expression product of a gene encoding the amino acid sequence of SEQ ID NO: 2, does not reasonably provide enablement for practicing the methods of claims 32, 38-40, 42, 43, 45-56, as presently claimed. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to

practice the invention commensurate in scope with these claims for the reasons set forth in section 15 of the previous Office action.

At pages 21-23 of the amendment filed August 17, 2004, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Firstly, as noted above, the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility for the reasons set forth in section 9 above, one skilled in the art clearly would not know how to use the claimed invention.

However, *were* the specification enabling for practicing the methods of claims 32, 38-40, 42, 43, 45-56, wherein said method comprises determining the expression of a nucleic acid molecule comprising SEQ ID NO: 1 or an expression product of a gene encoding the amino acid sequence of SEQ ID NO: 2, the skilled artisan could not use the claimed invention without the need to first perform an undue amount of additional experimentation to determine if variants of the gene encoding the polypeptide of SEQ ID NO: 2 are associated with the incidence, onset, or presence of colorectal cancer and whether the expression level of the variants can be used diagnostically. As evidenced by Skolnick et al., the skilled artisan cannot predict whether variants of a polypeptide, which are encoded by variants of a gene, will have the same function as the polypeptide or gene. The association of the expression level of a gene and the incidence, onset, or presence of colorectal cancer can only be determined empirically. Therefore, because the specification fails to provide adequate guidance, direction, and exemplification that is reasonably commensurate in scope with the claims, and because the art is unpredictable in nature, the skilled artisan could not use the claimed invention to diagnose colorectal cancer without the need to first perform an undue amount of additional experimentation to determine whether there is a correlation between the expression level of any one variant of the gene encoding the polypeptide of SEQ ID NO: 2 and the incidence, onset, or presence of colorectal cancer in a patient.

Applicant has argued that Skolnick et al. does not explicitly address the inability to reliably and accurately predict whether a protein that is 90% identical to another protein having a known function will also have that same function; nonetheless, the art is unpredictable, and it does not matter whether a variant of a protein is 90% identical or only 40% identical, because one cannot extrapolate the function of a variant, given only knowledge of the similarity between the variant and another protein having a known function. Applicant has contrarily asserted that if a protein having a known function and a variant of the protein are 90% identical, the skilled artisan can reliably and accurately predict the function of the variant, but notably Applicant has not provided any factual evidence to support this assertion. Thus, there is a preponderance of evidence of record that the skilled artisan could not use the claimed invention without the need to first perform an undue amount of additional experimentation.

11. The rejection of claims 32, 38-40, 42, 43, and 45-56 under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for a reason set forth in section 16 of the previous Office action is maintained. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

At pages 23 and 24 of the amendment filed August 17, 2004, Applicant has traversed this ground of rejection.

Applicant's arguments have been carefully considered but not found persuasive for the following reasons:

Applicant's amendment has obviated part of the ground of rejection set forth in the previous Office action, since the present claims are drawn to a method comprising "detecting" the level of expression of a polynucleotide encoding a CBF9 polypeptide, which is an RNA equivalent of a nucleic acid molecule having a polynucleotide sequence that is at least 90% identical to SEQ ID NO: 2.

Nevertheless, as previously noted, the claims are interpreted to encompass a method comprising determining the expression of an RNA equivalent of a nucleic acid

encoding a CBF9 polypeptide that comprises a polynucleotide sequence that is "at least 90% identical" to SEQ ID NO: 1. The disclosure, however, includes only an adequate description of a nucleic acid molecule having the polynucleotide sequence set forth in SEQ ID NO: 1.

In accordance with the *Guidelines*, which were cited in the previous Office action, because the art is unpredictable, as evidenced by Sknolnick et al., SEQ ID NO: 1 is not considered representative of the genus of nucleic acid molecules encoding a CBF9 polypeptide and comprising a polynucleotide sequence that is at least 90% identical to SEQ ID NO: 1, as a whole. Factual evidence of an actual reduction to practice has not been disclosed by Applicant in the specification; nor has Applicant shown the invention was "ready for patenting" by disclosure of drawings or structural chemical formulas that show that the invention was complete. As only the structure of SEQ ID NO: 1 is adequately described, the specification does not include an adequate description of at least a representative number of members of the genus of genes to which the claims refer. Applicant has not described distinguishing identifying characteristics sufficient to show that Applicant was in possession of the claimed invention at the time the application was filed, because the specification does not disclose a correlation between the recited common structural feature of the members of the genus of genes to which the claims refer, i.e., having a polynucleotide sequence that is at least 90% identical to SEQ ID NO: 1, and any particular function. Accordingly, the written description of the claimed invention would not reasonably convey to the skilled artisan that Applicant had possession of the claimed invention at the time the application was filed.

***New Grounds of Objection***

12. Claims 32, 38-40, and 42-56 are objected to because claims 32 and 50 recite, "detecting the level of expression". A level of expression can be measured, but it cannot be detected. Appropriate correction is required.

13. Claims 32, 38-40, and 42-56 are objected to because claims 32 and 50 recite, "indicative of cancer" in the last line(s) of the claims, where the claims are drawn to a

method for diagnosing "colorectal cancer", as opposed to any type of cancer. Appropriate correction is required.

14. Claims 50-56 are objected to because claim 50 recites a step denoted as (a) without reciting an additional step. Appropriate correction is required.

### *New Grounds of Rejection*

15. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

16. Claims 57-59 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 57-59 are indefinite because the claim 57 does not recite a positive process step that clearly relates back to the purpose of the invention recited in the preamble of the claim. Claim 57 recites a step of measuring the level of expression of an expression product of a gene in a patient and comparing that level of expression to the level of expression of the same expression product of a gene in a normal human, but the claim fails to provide a correlative step that might provide an indication of whether colorectal cancer is present in the patient. The skilled artisan would therefore not be reasonably apprised of the metes and bounds of the subject matter that Applicant regards as the invention.

### *Conclusion*

17. No claims are allowed.

18. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

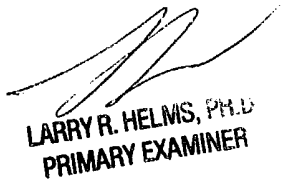
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

19. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Stephen L. Rawlings, Ph.D. whose telephone number is (571) 272-0836. The examiner can normally be reached on Monday-Friday, 8:30AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on (571) 272-0787. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Stephen L. Rawlings, Ph.D.
Examiner
Art Unit 1642




slr
November 4, 2004